

I. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-34 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner states:

The claims are drawn to multivesicular liposomes (MLV) prepared by the recited method which comprises, among other steps, one step wherein a "first aqueous component" is added in making a water-in-oil emulsion and another step wherein a "second aqueous" component is added. However, nowhere in the specification [is there sic] to be found a clear description what constitutes the "first aqueous component" and the "second aqueous component".

(Office Action at page 3). Applicants respectfully traverse this rejection.

Applicants submit that the term "aqueous" is well recognized in the art and has a distinctive meaning (i.e., of a water-miscible solvent). Any aqueous component appropriate for making liposomes may be used and many have been previously disclosed in the art. Any person having ordinary skill in the art would readily recognize the types of appropriate aqueous components that could be used for either the first or second components. Furthermore, the first aqueous component is further defined at page 5, line 6 and page 6, fourth line from the bottom, as comprising a biologically active substance.

Applicants submit that the second aqueous component is described in Examples 1 and 2, pages 11 and 13, at step 4. Thus, the first and second aqueous components may be identical or different, except that the first aqueous component will also comprise a biologically active substance. Applicants believe that the terms "first aqueous component" and "second aqueous component" are readily identifiable by those skilled in the art with reference to the present disclosure.

Applicants additionally submit that one skilled in the art with reference to the specification would identify the relationship and composition of the first and second aqueous components. Thus, Applicants submit that the first and second "aqueous components" are sufficiently defined and enabled by the specification and to those of skill in the art. Accordingly, Applicants respectfully request reconsideration and withdrawal of the §112, first paragraph rejection.

Additionally, Claims 1-34 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to practice the claimed invention.

The Examiner states in part, "... one having ordinary skill in the art would not be able to practice the invention because they would not know what to use as the aqueous component that would yield the multivesicular liposomes with the defined morphological characteristics." (Office Action at page 4). Applicants respectfully traverse this rejection.

As stated *supra*, Applicants submit that one of skill in the art would be able to readily identify aqueous compositions that can be used in the present invention. For example, Applicants submit that the term "aqueous" is well recognized in the art and has a distinctive meaning (i.e., of a water-miscible solvent), and many aqueous compositions useful for making liposomes have previously been established in the art and are well known. Furthermore, the aqueous component is further defined at page 5, line 6 and page 6, fourth line from the bottom, as comprising a biologically active substance.

Applicants submit that the second aqueous component is described in Examples 1 and 2, pages 11 and 13, at step 4. Applicants believe that the terms "first aqueous component" and "second aqueous component" are readily identifiable by those skilled in the art with reference to the present disclosure. Applicants also respectfully submit that it would not require undue experimentation to identify aqueous components that can be used in the present invention to obtain multivesicular liposomes having the morphological characteristics of Applicants invention.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976); MPEP §2164.01. It would only require routine experimentation using the process disclosed and claimed by Applicants to identify aqueous components. "The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (citing, *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 218 (CCPA 1976)). Thus, Applicants respectfully submit that the present invention is sufficiently enabled to one of skill in the art with reference to the present specification and would not require undue experimentation to identify

aqueous components and to practice the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the §112, first paragraph rejection.

II. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 1-34 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which application regards as the invention.

The Examiner states in the rejection, "The expression "nonhydrohalic acid" is vague and indefinite in the absence of specifying the intended acid." (Office Action at page 4). Applicants respectfully traverse this rejection.

Definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP §2173.02. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. MPEP §2173.02.

In this regard, Applicants respectfully direct the Examiner to page 7, second full paragraph, in which Applicants list a number of nonhydrohalic acids. Additionally, the Applicants respectfully direct the Examiner to page 6, where Applicants recite a list of hydrohalic acids. Thus, Applicants submit that the claim are not indefinite in light of the specification. For example, upon reading the specification one would be able to readily identify hydrohalic acids as well as a list of non-hydrohalic acids. Accordingly, Applicants respectfully request that the §112, second paragraph rejection be withdrawn.


In summary, for the reasons set forth herein, Applicants maintain that claims 1-35 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action and allow the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (619) 678-5070.

Please charge any additional fees, or make any credits, to Deposit Account No.
06-1050.

Respectfully submitted,

Date: 3/29/99


John R. Wetherell, Jr., Ph.D.
Reg. No. 31,678

Fish & Richardson P.C.
4225 Executive Square, Suite 1400
La Jolla, CA 92037
Telephone: 619/678-5070
Facsimile: 619/678-5099
83220.LJI